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frequency  
NEWS 5 Feb 19 Access via Tymnet and SprintNet Eliminated Effective 3/31/02  
NEWS 6 Mar 08 Gene Names now available in BIOSIS  
NEWS 7 Mar 22 TOXLIT no longer available  
NEWS 8 Mar 22 TRCTHERMO no longer available  
NEWS 9 Mar 28 US Provisional Priorities searched with P in CA/CAPplus  
and USPATFULL  
NEWS 10 Mar 28 LIPINSKI/CALC added for property searching in REGISTRY  
NEWS 11 Apr 02 PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.  
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NEWS 13 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area  
NEWS 14 Apr 09 ZDB will be removed from STN  
NEWS 15 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB  
NEWS 16 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS  
NEWS 17 Apr 22 BIOSIS Gene Names now available in TOXCENTER  
NEWS 18 Apr 22 Federal Research in Progress (FEDRIP) now available  
NEWS 19 Jun 03 New e-mail delivery for search results now available  
NEWS 20 Jun 10 MEDLINE Reload  
NEWS 21 Jun 10 PCTFULL has been reloaded

**NEWS EXPRESS** February 1 CURRENT WINDOWS VERSION IS V6.0d,  
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0ja(JP),  
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002  
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**NEWS INTER** General Internet Information  
**NEWS LOGIN** Welcome Banner and News Items  
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FILE 'EMBASE' ENTERED AT 13:24:18 ON 12 JUN 2002  
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FILE 'BIOSIS' ENTERED AT 13:24:18 ON 12 JUN 2002  
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC. (R)

=> s hillman J?/au or Guegler K?/au or Patterson C?/au  
L1 3870 HILLMAN J?/AU OR GUEGLER K?/AU OR PATTERSON C?/AU

=> s 11 and protease?  
L2 80 L1 AND PROTEASE?

=> S 12 AND GROWTH?  
L3 15 L2 AND GROWTH?

=> dup rem l3  
PROCESSING COMPLETED FOR L3  
L4 7 DUP REM L3 (8 DUPLICATES REMOVED)

-> dis 14 1-7 ibib abs kwic

ANSWER 1 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

L4 ANSWER 1 OF 7 BIOSIS CORP.  
ACCESSION NUMBER: 2001:499589 BIOSIS  
DOCUMENT NUMBER: PREV200100499589  
TITLE: Growth-associated protease inhibitor  
heavy chain precursor.  
AUTHOR(S): Hillman, Jennifer L.; Guegler, Karl J.  
Patterson, Chandra

PATENT INFORMATION: US 6228991 May 08, 2001  
ASSIGNEE: Incyte Genomics, Inc.  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (May 8, 2001) Vol. 1246, No. 2, pp. No

Office of the Commissioner for Patents  
Pagination. e-file.  
ISSN: 0098-1133.

**protease inhibitor heavy chain precursor (GAPIP)** and polynucleotides which identify and encode GAPIP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders associated with expression of GAPIP.

TI Growth-associated protease inhibitor heavy chain precursor.

AU Hillman, Jennifer L.; Guegler, Karl J.;

Patterson, Chandra

AB The invention provides a human growth-associated protease inhibitor heavy chain precursor (GAPIP) and polynucleotides which identify and encode GAPIP. The invention also provides expression vectors, host cells, . . .

IT Molecular Genetics (Biochemistry and Molecular Biophysics); Methods and Techniques; Pharmacology

IT Diseases GAPIP expression-associated disorders: disease-miscellaneous

IT Chemicals & Biochemicals growth-associated protease inhibitor heavy chain precursor [GAPIP]; polynucleotides

L4 ANSWER 2 OF 7 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2001665722 MEDLINE

DOCUMENT NUMBER: 21567998 PubMed ID: 11711494

TITLE: Cyclic strain increases protease-activated receptor-1 expression in vascular smooth muscle cells.

AUTHOR: Nguyen K T; Frye S R; Eskin S G; Patterson C;

Runge M S; McIntire L V

CORPORATE SOURCE: Department of Bioengineering, Rice University, Houston, Texas, USA..

CONTRACT NUMBER: HL-03658 (NHLBI)

HL-18672 (NHLBI)

HL-57352 (NHLBI)

NS-23327 (NINDS)

SOURCE: HYPERTENSION, (2001 Nov) 38 (5) 1038-43.

Journal code: 7906255. ISSN: 1524-4563.

(Investigators: McIntire L V, Rice U, Houston, TX)

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals; Space Life Sciences

ENTRY MONTH: 200112

ENTRY DATE: Entered STN: 20011119

Last Updated on STN: 20020131

Entered Medline: 20011207

AB Cyclic strain regulates many vascular smooth muscle cell (VSMC) functions through changing gene expression. This study investigated the effects of cyclic strain on protease-activated receptor-1 (PAR-1) expression in VSMCs and the possible signaling pathways involved, on the basis of the hypothesis that cyclic strain would enhance PAR-1 expression, reflecting increased thrombin activity. Uniaxial cyclic strain (1 Hz, 20% of cells cultured on elastic membranes induced a 2-fold increase in both PAR-1 mRNA and protein levels. Functional activity of PAR-1, as assessed by cell proliferation in response to thrombin, was also increased by cyclic strain. In addition, treatment of cells with antioxidants or an NADPH oxidase inhibitor blocked strain-induced PAR-1 expression. Preincubation of cells with protein kinase inhibitors (staurosporine or Ro 31-8220) enhanced strain-increased PAR-1 expression, whereas inhibitors of NO synthase, tyrosine kinase, and mitogen-activated protein kinases had no effect. Cyclic strain in the presence of basic fibroblast growth factor induced PAR-1 mRNA levels beyond the effect of cyclic strain alone, whereas no additive effect was observed between cyclic strain and platelet-derived growth factor-AB. Our findings that cyclic strain upregulates PAR-1 mRNA expression but that shear stress downregulates this gene in VSMCs provide an opportunity to elucidate signaling differences by which VSMCs respond to different mechanical forces.

TI Cyclic strain increases protease-activated receptor-1 expression in vascular smooth muscle cells.

AU Nguyen K T; Frye S R; Eskin S G; Patterson C; Runge M S;

McIntire L V

AB . . . many vascular smooth muscle cell (VSMC) functions through changing gene expression. This study investigated the effects of cyclic strain on protease-activated receptor-1 (PAR-1) expression in VSMCs and the possible signaling pathways involved, on the basis of the hypothesis that cyclic strain . . . of NO synthase, tyrosine kinase, and mitogen-activated protein kinases had no effect. Cyclic strain in the presence of basic fibroblast growth factor induced PAR-1 mRNA levels beyond the effect of cyclic strain alone, whereas no additive effect was observed between cyclic strain and platelet-derived growth factor-AB. Our findings that cyclic strain upregulates PAR-1 mRNA expression but that shear stress downregulates this gene in VSMCs provide. . .

CT . . . Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Aorta: ME, metabolism

Cell Division: DE, drug effects

Cells, Cultured

Enzyme Inhibitors: PD, pharmacology

Growth Substances: PD, pharmacology

Muscle, Smooth, Vascular: DE, drug effects

\*Muscle, Smooth, Vascular: ME, metabolism

Nitric-Oxide Synthase: PH, physiology

Oxidative. . .

CN 0 (Enzyme Inhibitors); 0 (Growth Substances); 0 (RNA, Messenger); 0 (Reactive Oxygen Species); 0 (Receptors, Thrombin); 0 (protease-activated receptor 1); EC 1.14.13.39 (Nitric-Oxide Synthase); EC 2.7.1.37 (Protein Kinases); EC 3.4.21.5 (Thrombin)

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:887825 CAPLUS

DOCUMENT NUMBER: 136:148338

TITLE: Cyclic strain increases protease-activated receptor-1 expression in vascular smooth muscle cells

AUTHOR(S): Nguyen, Kyatia T.; Frye, Stacie R.; Eskin, Suzanne G.; Patterson, Cam; Runge, Marschall S.; McIntire, Larry V.

CORPORATE SOURCE: Department of Bioengineering, Rice University, Houston, TX, 77251-1892, USA

SOURCE: Hypertension (2001), 38(5), 1038-1043

CODEN: HPRTDN; ISSN: 0194-911X

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cyclic strain regulates many vascular smooth muscle cell (VSMC) functions through changing gene expression. This study investigated the effects of cyclic strain on protease-activated receptor-1 (PAR-1) expression in VSMCs and the possible signaling pathways involved, on the basis of the hypothesis that cyclic strain would enhance PAR-1 expression, reflecting increased thrombin activity. Uniaxial cyclic strain (1 Hz, 20%) of cells cultured on elastic membranes induced a 2-fold increase in both PAR-1 mRNA and protein levels. Functional activity of PAR-1, as assessed by cell proliferation in response to thrombin, was also increased by cyclic strain. In addn., treatment of cells with antioxidants or an NADPH oxidase inhibitor blocked strain-induced PAR-1 expression. Preincubation of cells with protein kinase inhibitors (staurosporine or Ro 31-8220) enhanced strain-increased PAR-1 expression, whereas inhibitors of NO synthase, tyrosine kinase, and mitogen-activated protein kinases had no effect. Cyclic strain in the presence of basic fibroblast growth factor induced PAR-1 mRNA levels beyond the effect of cyclic strain alone, whereas no additive effect was obstd. between cyclic strain and platelet-derived growth factor-AB. These findings that cyclic strain upregulates PAR-1 mRNA expression but that shear stress downregulates this gene in VSMCs provide an opportunity to elucidate signaling differences by which VSMCs respond to different mech. forces.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Cyclic strain increases protease-activated receptor-1 expression

AU Nguyen, Kyat T.; Frye, Stacie R.; Eskin, Suzanne G.; Patterson, Cam; Runge, Marshall S.; McIntire, Larry V.

AB Cyclic strain regulates many vascular smooth muscle cell (VSMC) functions through changing gene expression. This study investigated the effects of cyclic strain on protease-activated receptor-1 (PAR-1) expression in VSMCs and the possible signaling pathways involved, on the basis of the hypothesis that cyclic strain would enhance PAR-1 expression, reflecting increased thrombin activity. Uniaxial cyclic strain (1 Hz, 20%) of cells cultured on elastic membranes induced a 2-fold increase in both PAR-1 mRNA and protein levels. Functional activity of PAR-1, as assessed by cell proliferation in response to thrombin, was also increased by cyclic strain. In addn., treatment of cells with antioxidants or an NADPH oxidase inhibitor blocked strain-induced PAR-1 expression. Preincubation of cells with protein kinase inhibitors (staurosporine or Ro 31-8220) enhanced strain-increased PAR-1 expression, whereas inhibitors of NO synthase, tyrosine kinase, and mitogen-activated protein kinases had no effect. Cyclic strain in the presence of basic fibroblast growth factor induced PAR-1 mRNA levels beyond the effect of cyclic strain alone, whereas no additive effect was obstd. between cyclic strain and platelet-derived growth factor-AB. These findings that cyclic strain upregulates PAR-1 mRNA expression but that shear stress downregulates this gene in VSMCs provide an opportunity to elucidate signaling differences by which VSMCs respond to different mech. forces.

ST strain stress protease activated receptor 1 vascular smooth

muscle

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(PAR-1 (proteinase-activated receptor 1); cyclic strain increases  
protease-activated receptor-1 expression in vascular smooth  
muscle cells)

IT Human

Shear stress

Signal transduction, biological

Strain

(cyclic strain increases protease-activated receptor-1  
expression in vascular smooth muscle cells)

IT Oxidative stress, biological

(cyclic strain increases protease-activated receptor-1  
expression in vascular smooth muscle cells in relation to oxidative  
stress)

IT Blood vessel

(smooth muscle; cyclic strain increases protease-activated  
receptor-1 expression in vascular smooth muscle cells)

IT 77106-92-4, NAD(P)H oxidase 80449-02-1, Protein kinase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cyclic strain increases protease-activated receptor-1  
expression in vascular smooth muscle cells)

IT 106096-93-9, Basic fibroblast growth factor

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cyclic strain increases protease-activated receptor-1  
expression in vascular smooth muscle cells in relation to fibroblast  
growth factor)

IT 9002-04-4, Thrombin

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cyclic strain increases protease-activated receptor-1  
expression in vascular smooth muscle cells in relation to thrombin)

L4 ANSWER 4 OF 7 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 2001109938 MEDLINE

DOCUMENT NUMBER: 20525510 PubMed ID: 11071917

TITLE: Developmental regulation of FKBP65. An ER-localized extracellular matrix binding-protein.

AUTHOR: Patterson C E; Schaub T; Coleman E J; Davis E C

CORPORATE SOURCE: Department of Cell Biology, University of Texas Southwestern Medical Center, Dallas, Texas 75390, USA.

CONTRACT NUMBER: HL-60394 (NHLBI)

SOURCE: MOLECULAR BIOLOGY OF THE CELL, (2000 Nov) 11 (11) 3925-35.

JOURNAL code: 9201390. ISSN: 1059-1524.

PUB. COUNTRY: United States

JOURNAL; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200102

ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322

Entered Medline: 20010202

AB FKBP65 (65-kDa FK506-binding protein) is a member of the highly conserved family of intracellular receptors called immunophilins. All have the property of peptidyl-prolyl cis-trans isomerization, and most have been implicated in folding and trafficking events. In an earlier study, we identified that FKBP65 associates with the extracellular matrix protein tropoelastin during its transport through the cell. In the present study, we have carried out a detailed investigation of the subcellular localization of FKBP65 and its relationship to tropoelastin. Using subcellular fractionation, Triton X-114 phase separation, protease protection assays, and immunofluorescence microscopy (IF), we have identified that FKBP65 is contained within the lumen of the endoplasmic

reticulum (ER). Subsequent IF studies colocalized FKBP65 with tropoelastin and showed that the two proteins dissociate before reaching the Golgi apparatus. Immunohistochemical localization of FKBP65 in developing lung showed strong staining of vascular and airway smooth muscle cells. Similar areas stained positive for the presence of elastic fibers in the extracellular matrix. The expression of FKBP65 was investigated during development as tropoelastin is not expressed in adult tissues. Tissue-specific expression of FKBP65 was observed in 12-d old mouse tissues; however, the pattern of expression of FKBP65 was not restricted to those tissues expressing tropoelastin. This suggests that additional ligands for FKBP65 likely exist within the ER. Remarkably, in the adult tissues examined, FKBP65 expression was absent or barely detectable. Taken together, these results support an ER-localized FKBP65-tropoelastin interaction that occurs specifically during growth and development of tissues.

AU Patterson C E; Schaub T; Coleman E J; Davis E C  
 AB . . . detailed investigation of the subcellular localization of FKBP65 and its relationship to tropoelastin. Using subcellular fractionation, Triton X-114 phase separation, protease protection assays, and immunofluorescence microscopy (IF), we have identified that FKBP65 is contained within the lumen of the endoplasmic reticulum. . . . FKBP65 expression was absent or barely detectable. Taken together, these results support an ER-localized FKBP65-tropoelastin interaction that occurs specifically during growth and development of tissues.

CT Reticulum: ME, metabolism

\*Extracellular Matrix: ME, metabolism  
 Gene Expression Regulation, Developmental  
 Golgi Apparatus: ME, metabolism  
 Intracellular Membranes  
 Lung: CY, cytology  
 \*Lung: GD, growth & development  
 Lung: ME, metabolism  
 Mice  
 Molecular Sequence Data  
 Muscle, Smooth: ME, metabolism  
 Tacrolimus Binding Proteins: GE, genetics

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:723056 CAPLUS  
 DOCUMENT NUMBER: 131:333062  
 TITLE: sequence and therapeutic applications for human  
 growth-associated protease inhibitor  
 heavy chain precursor  
 INVENTOR(S): Hillman, Jennifer L.; Guegler, Karl  
 J.; Patterson, Chandra  
 PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 92 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9957140	A2	19991111	WO 1999-US9947	19990505
WO 9957140	A3	19991229		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6001596	A	19991214	US 1998-74579	19980507
CA 2328132	AA	19991111	CA 1999-2328132	19990505
AU 9938867	A1	19991123	AU 1999-38867	19990505
EP 1078062	A2	20010228	EP 1999-921739	19990505
R: BE, DE, ES, FR, GB, IT, NL				
JP 2002513553	T2	20020514	JP 2000-547109	19990505
US 6228991	B1	20010508	US 1999-388774	19990502
PRIORITY APPLN. INFO.:			US 1998-74579	A2 19980507
			WO 1999-US9947	W 19990505

AB The invention provides a human growth-assoccd. protease inhibitor heavy chain precursor (GAPIP) and polynucleotides which identify and encode GAPIP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders involving the reproductive tract or immunol. disorder or developmental or neoplastic disorders assoccd. with expression of GAPIP. An assay for identification of mols. which interact with GAPIP is described.

TI sequence and therapeutic applications for human growth-assoccd. protease inhibitor heavy chain precursor

IN Hillman, Jennifer L.; Guegler, Karl J.; Patterson, Chandra

AB The invention provides a human growth-assoccd. protease inhibitor heavy chain precursor (GAPIP) and polynucleotides which identify and encode GAPIP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders involving the reproductive tract or immunol. disorder or developmental or neoplastic disorders assoccd. with expression of GAPIP. An assay for identification of mols. which interact with GAPIP is described.

ST therapy sequence human growth protease inhibitor heavy chain

IT Nucleic acid hybridization  
 (DNA-DNA; sequence and therapeutic applications for human growth-assoccd. protease inhibitor heavy chain precursor)

IT Immunity  
 Reproduction, animal  
 (disorder; sequence and therapeutic applications for human growth-assoccd. protease inhibitor heavy chain precursor)

IT Antitumor agents  
 Diagnosis  
 Drug delivery systems  
 Genetic vectors  
 Protein sequences  
 cDNA sequences

(sequence and therapeutic applications for human growth  
-assocd. protease inhibitor heavy chain precursor)

IT Antibodies  
Probes (nucleic acid)  
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);  
ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(sequence and therapeutic applications for human growth  
-assocd. protease inhibitor heavy chain precursor)

IT 249916-69-6  
RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; sequence and therapeutic applications for human  
growth-assocd. protease inhibitor heavy chain  
precursor)

IT 249916-73-2  
RL: BSU (Biological study, unclassified); PRP (Properties); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(nucleotide sequence; sequence and therapeutic applications for human  
growth-assocd. protease inhibitor heavy chain  
precursor)

IT 249760-99-4, PN: WO9957140 SEQID: 3 unclaimed protein 249761-00-0, PN:  
WO9957140 SEQID: 4 unclaimed protein 249761-01-1, PN: WO9957140 SEQID: 5  
unclaimed protein  
RL: PRP (Properties)  
(unclaimed protein sequence; sequence and therapeutic applications for  
human growth-assocd. protease inhibitor heavy chain  
precursor)

L4 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2000:282931 BIOSIS  
DOCUMENT NUMBER: PREV200000282931  
TITLE: Growth-associated protease inhibitor  
heavy chain precursor.  
AUTHOR(S): Hillman, Jennifer L.; Guegler, Karl J.;  
Patterson, Chandr  
ASSIGNEE: Incyte Pharmaceuticals, Inc.  
PATENT INFORMATION: US 6001596 December 14, 1999  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Dec. 14, 1999) Vol. 1229, No. 2, pp. No  
pagination. e-file.  
ISSN: 0098-1133.

DOCUMENT TYPE: Patent  
LANGUAGE: English

AB The invention provides a human growth-associated  
protease inhibitor heavy chain precursor (GAPIP) and  
polynucleotides which identify and encode GAPIP. The invention also  
provides expression vectors, host cells, antibodies, agonists, and  
antagonists. The invention also provides methods for diagnosing, treating  
or preventing disorders associated with expression of GAPIP.

TI Growth-associated protease inhibitor heavy chain  
precursor.

AU Hillman, Jennifer L.; Guegler, Karl J.;  
Patterson, Chandr

AB The invention provides a human growth-associated  
protease inhibitor heavy chain precursor (GAPIP) and  
polynucleotides which identify and encode GAPIP. The invention also  
provides expression vectors, host cells,.. .

IT Major Concepts  
Enzymology (Biochemistry and Molecular Biophysics); Human Medicine  
(Medical Sciences)

IT Chemicals & Biochemicals  
growth-associated protease inhibitor heavy chain  
precursor [GAPIP]: enzyme inhibitor

L4 ANSWER 7 OF 7 MEDLINE  
ACCESSION NUMBER: 89350177 MEDLINE  
DOCUMENT NUMBER: 89350177 PubMed ID: 2669631  
TITLE: Regulation of neurotoxin and protease formation  
in Clostridium botulinum Okra B and Hall A by arginine.  
AUTHOR: Patterson-Curtis S I; Johnson E A  
CORPORATE SOURCE: Department of Food Microbiology and Toxicology, University  
of Wisconsin, Madison 53706.  
SOURCE: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (1989 Jun) 55 (6)  
1544-8.  
Journal code: 7605801. ISSN: 0099-2240.

PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198909  
ENTRY DATE: Entered STN: 19900309  
Last Updated on STN: 19970203  
Entered Medline: 19890921

AB Supplementation of minimal medium with high levels of arginine (20  
g/liter) markedly decreased neurotoxin titers and protease  
activities in cultures of Clostridium botulinum Okra B and Hall A.  
Nitrogenous nutrients that are known to be derived from arginine,  
including proline, glutamate, and ammonia, also decreased protease  
and toxin but less so than did arginine. Proteases synthesized  
during growth were rapidly inactivated after growth  
stopped in media containing high levels of arginine. Separation of  
extracellular proteins by electrophoresis and immunoblots with antibodies  
to toxin showed that the decrease in toxin titers in media containing high  
levels of arginine was caused by both reduced synthesis of protoxin and  
impaired proteolytic activation. In contrast, certain other nutritional  
conditions stimulated protease and toxin formation in C.  
botulinum and counteracted the repression by arginine. Supplementation of  
minimal medium with casein or casein hydrolysates increased  
protease activities and toxin titers. Casein supplementation of a  
medium containing high levels of arginine prevented protease  
inactivation. High levels of glucose (50 g/liter) also delayed the  
inactivation of proteases in both the minimal medium and a  
medium containing high levels of arginine. These observations suggest that  
the availability of nitrogen and energy sources, particularly arginine,  
affects the production and proteolytic processing of toxins and  
proteases in C. botulinum.

TI Regulation of neurotoxin and protease formation in Clostridium  
botulinum Okra B and Hall A by arginine.

AU Patterson-Curtis S I; Johnson E A  
AB Supplementation of a minimal medium with high levels of arginine (20  
g/liter) markedly decreased neurotoxin titers and protease  
activities in cultures of Clostridium botulinum Okra B and Hall A.  
Nitrogenous nutrients that are known to be derived from arginine,

including proline, glutamate, and ammonia, also decreased protease and toxin but less so than did arginine. Proteases synthesized during growth were rapidly inactivated after growth stopped in media containing high levels of arginine. Separation of extracellular proteins by electrophoresis and immunoblots with antibodies to toxin. . . arginine was caused by both reduced synthesis of prototoxin and impaired proteolytic activation. In contrast, certain other nutritional conditions stimulated protease and toxin formation in *C. botulinum* and counteracted the repression by arginine. Supplementation of the minimal medium with casein or casein hydrolysates increased protease activities and toxin titers. Casein supplementation of a medium containing high levels of arginine prevented protease inactivation. High levels of glucose (50 g/liter) also delayed the inactivation of proteases in both the minimal medium and a medium containing high levels of arginine. These observations suggest that the availability of nitrogen and energy sources, particularly arginine, affects the production and proteolytic processing of toxins and proteases in *C. botulinum*.

=> dis his  
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FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 13:24:18 ON 12 JUN 2002  
L1 3870 S HILLMAN J?/AU OR GUEGLER K?/AU OR PATTERSON C?/AU  
L2 80 S L1 AND PROTEASE?  
L3 15 S L2 AND GROWTH?  
L4 2 DUD RRM L3 (8 DUPLICATES REMOVED)

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE    TOTAL
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FILE 'EMBASE' ENTERED AT 13:52:33 ON 12 JUN 2002  
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FILE 'BIOSIS' ENTERED AT 13:52:33 ON 12 JUN 2002  
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

=> s (protease (1N) inhibitor?)  
L1 70323 (PROTEASE (1N) INHIBITOR?)

=> s 11 (10N) growth  
L2 912 L1 (10N) GROWTH

=> s 12 (P) human?  
L3 212 L2 (P) HUMAN?

=> s 13 (P) sequence?  
L4 35 L3 (P) SEQUENCE?

=> dup rem 14  
PROCESSING COMPLETED FOR L4  
L5 15 DUP REM L4 (20 DUPLICATES REMOVED)

=> dis 15 1-15 ibib abs kwic

L5 ANSWER 1 OF 15 MEDLINE DUPLICATE 1  
ACCESSION NUMBER: 2002016001 MEDLINE  
DOCUMENT NUMBER: 21325286 PubMed ID: 11432724  
TITLE: Intracellular location and nuclear targeting of the Spi-1, Spi-2 and Spi-3 gene-derived serine protease inhibitors in non-secretory cells.  
AUTHOR: Rothbarth K; Kempf T; Juodka B; Glaser T; Stammer H; Werner D  
CORPORATE SOURCE: Division of Biochemistry of the Cell (B0300), German Cancer Research Center, Heidelberg.  
SOURCE: EUROPEAN JOURNAL OF CELL BIOLOGY, (2001 May) 80 (5) 341-8.  
JOURNAL CODE: 7906240. ISSN: 0171-9335.  
PUB. COUNTRY: Germany: Germany, Federal Republic of  
JOURNAL; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200112  
ENTRY DATE: Entered STN: 20020121  
Last Updated on STN: 20020121  
Entered Medline: 20011204

AB Proteases and their inhibitors are indispensable for the regulated activation and/or degradation of structural and functional proteins involved in basic cellular processes, e.g. in cell cycle control, cell growth, differentiation and apoptosis. In this context the serine protease inhibitors derived from the murine Spi-1, Spi-2 and Spi-3 genes, and their human homologs, deserve reconsideration. Microsequencing data indicate that a fraction of the three serpins has the capability to constitute a well characterized proteinase K, high salt and SDS-stable complex which coisolates with DNA under salting out conditions from various cell and tissue types. This tight association with DNA isolated under conditions designed to deproteinize DNA efficiently points to an in situ preformed chromatin complex. Accordingly, in addition to their well known functions as 'serum protease inhibitors' the Spi-1 and Spi-2 gene-derived proteins appear to have intracellular functions as well. The involvement of the three serpins in chromatin complexes requires their nuclear translocation. Application of (enhanced) green fluorescent protein technology and optical section microscopy reveals that truncation of the N-terminal signal sequences of the Spi-1 and Spi-2 gene-encoded proteins is a prerequisite for their nuclear translocation while non-truncated fusion proteins are enriched at the nuclear indentation which is the site of the Golgi apparatus and the centrosome. The identification of new species of intracellular serpins is of potential interest with respect to accumulating evidence for serine protease inhibitor-dependent inhibition or prevention of apoptosis.

AB . . . regulated activation and/or degradation of structural and functional proteins involved in basic cellular processes, e.g. in cell cycle control, cell growth, differentiation and apoptosis. In this context the serine protease inhibitors derived from the murine Spi-1, Spi-2 and Spi-3 genes, and their human homologs, deserve reconsideration. Microsequencing data indicate that a fraction of the three serpins has the capability to constitute a well . . . nuclear translocation. Application of (enhanced) green fluorescent protein technology and optical section microscopy reveals that truncation of the N-terminal signal sequences of the Spi-1 and Spi-2 gene-encoded proteins is a prerequisite for their nuclear translocation while non-truncated fusion proteins are enriched. . .

L5 ANSWER 2 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2002:186414 BIOSIS  
DOCUMENT NUMBER: PREV200200186414  
TITLE: Analysis of gene expression in a B cell neoplasm with the phenotype of a primary effusion lymphoma (PEL).  
AUTHOR(S): Parker, Charles J. (1); Vreeke, Teresa M.; Lin, Chen-Yong; Dickson, Robert B.  
CORPORATE SOURCE: (1) Medicine, VA Medical Center, Salt Lake City, UT USA  
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 302a. <http://www.bloodjournal.org/>. print.  
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001  
ISSN: 0006-4971.

DOCUMENT TYPE: Conference  
LANGUAGE: English

AB PEL is defined by the presence of a lymphomatous effusion in the absence of an identifiable contiguous tumor mass. In most instances, the malignant cells are infected with both Epstein Barr virus (EBV) and human herpes virus-8 (HHV-8). In a minority of cases, the lymphoma cells are infected with either EBV or HHV-8. When infected with EBV, t(8;14) is invariably present, but this translocation is not observed if the cells are infected with HHV-8. To gain insight into the molecular basis of the unique phenotype, the pattern of gene expression in cells derived from a

patient with the clinical characteristics of PEL was analyzed. The malignant cells were cultured from the pleural fluid of an elderly HIV-negative man. Immunophenotyping was consistent with a lambda light-chain restricted B cell neoplasm of follicular center cell origin. Multiple cytogenetic abnormalities, including t(8;14) were observed in the lymphoma cells. Representation difference analysis (RDA) of DNA revealed fragments of the EBV genome in the tumor cells but HHV-8 DNA was absent by both RDA and PCR analysis. By using RDA modified for cDNA, the pattern of gene expression of the lymphoma cells was compared to that of the patient's peripheral blood B cells immortalized with EBV. A combination of Southern, northern, and sequence analysis showed that 12/40 clones from the tumor sample matched the cDNA of matriptase, a protease that degrades extracellular matrix and is implicated in tumor invasion and metastasis. In addition, matriptase was shown to activate urokinase-type plasminogen activator, hepatocyte growth factor, and protease activated receptor-2. In all tissues examined previously (both normal and malignant), matriptase was invariably co-expressed along with its cognate inhibitor, hepatic growth factor activator inhibitor-1 (HAI-1).

This Kunitz-type serine protease inhibitor is a type I integral membrane protein that regulates matriptase by binding to the activated protein on the cell surface with subsequent shedding of the ectodomain of the complex. Analysis by both flow cytometry and western blot using monoclonal antibodies demonstrated that the PEL cells expressed matriptase protein but not its cognate inhibitor, HAI-1. In contrast, the control cell line expressed HAI-1 but not matriptase. This case appears to be the first reported instance in which matriptase is expressed in the absence of its cognate inhibitor. Because of its potential role in degradation of extracellular matrix, tumor invasion, metastasis, and activation of growth factors and other proteins relevant to the malignant process, we postulate that unregulated expression of matriptase contributed to the unique clinical phenotype of this unusual B cell neoplasm.

AB . . . an identifiable contiguous tumor mass. In most instances, the malignant cells are infected with both Epstein Barr virus (EBV) and human herpes virus-8 (HHV-8). In a minority of cases, the lymphoma cells are infected with either EBV or HHV-8. When infected . . . was compared to that of the patient's peripheral blood B cells immortalized with EBV. A combination of Southern, northern, and sequence analysis showed that 12/40 clones from the tumor sample matched the cDNA of matriptase, a protease that degrades extracellular matrix. . . receptor-2. In all tissues examined previously (both normal and malignant), matriptase was invariably co-expressed along with its cognate inhibitor, hepatic growth factor activator inhibitor-1 (HAI-1). This Kunitz-type serine protease inhibitor is a type I integral membrane protein that regulates matriptase by binding to the activated protein on the cell surface. . .

L5 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2000:727687 CAPLUS  
DOCUMENT NUMBER: 135:29659  
TITLE: The WFDC1 gene encoding ps20 localizes to 16q24, a region of LOH in multiple cancers  
AUTHOR(S): Larsen, Melinda; Ressler, Steven J.; Gerdes, Michael J.; Lu, Bing; Byron, Meg; Lawrence, Jeanne B.; Rowley, David R.  
CORPORATE SOURCE: Cell and Molecular Biology Program, Baylor College of Medicine, Houston, TX, 77030, USA  
SOURCE: Mammalian Genome (2000), 11(9), 767-773  
CODEN: MAMGEC; ISSN: 0938-8990  
PUBLISHER: Springer-Verlag New York Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB We previously identified ps20 protein as a secreted growth inhibitor and purified the protein from fetal rat prostate urogenital sinus mesenchymal cell conditioned medium. The rat cDNA was subsequently cloned, and ps20 was found to contain a WAP-type four-disulfide core motif, indicating it may function as a protease inhibitor. We now report cloning and characterization of the mouse ps20 gene (designated Wfdc1), the human homolog cDNA, and the human gene (designated WFDC1). Both the mouse and human WFDC1 genes consist of seven exons and encode resp. ps20 proteins sharing 79.1% identity and nearly identical WAP motifs in exon 2. The WFDC1 gene was mapped by FISH anal. to human Chromosome (Chr) 16q24, an area of frequent loss of heterozygosity (LOH) previously identified in multiple cancers including prostate, breast, hepatocellular, and Wilms' tumor. Identification and characterization of the WFDC1 gene may aid in better understanding the potential role of this gene and ps20 in prostate biol. and carcinogenesis.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

- IT Protein motifs  
(WAP signature motif; amino acid sequences and protein motifs of the human and mouse ps20 proteins, a secreted growth inhibitor with motifs indicating it may function as a protease inhibitor)
- IT Protein sequences  
(amino acid sequences and protein motifs of the human and mouse ps20 proteins, a secreted growth inhibitor with motifs indicating it may function as a protease inhibitor)
- IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(genes Wfdc1 and WFDC1; ps20 (prostate stromal 20); amino acid sequences and protein motifs of the human and mouse ps20 proteins, a secreted growth inhibitor with motifs indicating it may function as a protease inhibitor)
- IT Growth inhibitors, animal  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(genes Wfdc1 and WFDC1; amino acid sequences and protein motifs of the human and mouse ps20 proteins, a secreted growth inhibitor with motifs indicating it may function as a protease inhibitor)

L5 ANSWER 4 OF 15 MEDLINE  
ACCESSION NUMBER: 2000394500 MEDLINE  
DOCUMENT NUMBER: 20359916 PubMed ID: 10775503  
TITLE: Serpins identified as cell growth inhibitors in human plasma.  
AUTHOR: Yao J; Baecher-Allan C M; Sharon J  
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, Boston University School of Medicine, 715 Albany Street, Boston, Massachusetts, 02118, USA.

DUPPLICATE 2

SOURCE: MOLECULAR CELL BIOLOGY RESEARCH COMMUNICATIONS, (2000 Feb)  
 3 (2) 76-81.  
 Journal code: 100889076. ISSN: 1522-4724.

PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
 Priority Journals

FILE SEGMENT: 200008  
 ENTRY MONTH: Entered STN: 20000824  
 ENTRY DATE: Last Updated on STN: 20000824  
 Entered Medline: 20000815

AB We have identified a new factor, CFX, in human serum and plasma that inhibits the growth of cultured human and mouse cell lines. CFX was determined to be a negatively charged, hydrophobic glycoprotein, with a native molecular weight of 110-120 kDa and a minimal active subunit of 55 kDa. It is precipitated by 60% ammonium sulfate and is resistant to heat treatment at 100 degrees C for 30 min. CFX was purified from human plasma to a single band on a gel which retained the cell growth inhibitory activity. Amino acid sequence analysis of the CFX band revealed sequences from four human glycoproteins, alpha1-antichymotrypsin, Cl-esterase inhibitor, alpha1-antitrypsin, and alpha2-antiplasmin, all members of the superfamily of serpins. Of the four, Cl-esterase inhibitor was shown to be the most potent cell growth inhibitor. These results suggest that serpins may play a cell growth inhibitory role in vivo, in addition to their role as protease inhibitors.

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AB We have identified a new factor, CFX, in human serum and plasma that inhibits the growth of cultured human and mouse cell lines. CFX was determined to be a negatively charged, hydrophobic glycoprotein, with a native molecular weight of . . . 60% ammonium sulfate and is resistant to heat treatment at 100 degrees C for 30 min. CFX was purified from human plasma to a single band on a gel which retained the cell growth inhibitory activity. Amino acid sequence analysis of the CFX band revealed sequences from four human glycoproteins, alpha1-antichymotrypsin, Cl-esterase inhibitor, alpha1-antitrypsin, and alpha2-antiplasmin, all members of the superfamily of serpins. Of the four, Cl-esterase inhibitor was shown to be the most potent cell growth inhibitor. These results suggest that serpins may play a cell growth inhibitory role in vivo, in addition to their role as protease inhibitors.

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L5 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:723056 CAPLUS  
 DOCUMENT NUMBER: 131:333062  
 TITLE: sequence and therapeutic applications for  
 human growth-associated  
 protease inhibitor heavy chain  
 precursor  
 INVENTOR(S): Hillman, Jennifer L.; Guegler, Karl J.; Patterson,  
 Chandra  
 PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 92 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9957140	A2	19991111	WO 1999-US9947	19990505
WO 9957140	A3	19991229		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG	A	19991214	US 1998-74579	19980507
US 6001596	A	19991111	CA 1999-2328132	19990505
CA 2328132	AA	19991111	AU 1999-38867	19990505
AU 9938867	A1	19991123	EP 1999-921739	19990505
EP 1078062	A2	20010228		
R: BE, DE, ES, FR, GB, IT, NL				
JP 2002513553	T2	20020514	JP 2000-547109	19990505
US 6228991	B1	20010508	US 1999-388774	19990902
US 1998-74579	A2		US 1998-74579	19980507
PRIORITY APPLN. INFO.:			WO 1999-US9947	W 19990505

AB The invention provides a human growth-assoccd. protease inhibitor heavy chain precursor (GAPIP) and polynucleotides which identify and encode GAPIP. The invention also provided expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating or preventing disorders involving the reproductive tract or immunol. disorder or developmental or neoplastic disorders assoccd. with expression of GAPIP. An assay for identification of mols. which interact with GAPIP is described.

TI sequence and therapeutic applications for human  
 growth-associated protease inhibitor heavy  
 chain precursor

ST therapy sequence human growth  
 protease inhibitor heavy chain

IT Nucleic acid hybridization  
 (DNA-DNA; sequence and therapeutic applications for  
 human growth-assoccd. protease  
 inhibitor heavy chain precursor)

IT Immunity  
 Reproduction, animal  
 (disorder; sequence and therapeutic applications for  
 human growth-assoccd. protease  
 inhibitor heavy chain precursor)

IT Antitumor agents  
 Diagnosis  
 Drug delivery systems  
 Genetic vectors  
 Protein sequences  
 cDNA sequences  
 (sequence and therapeutic applications for human  
 growth-assoccd. protease inhibitor heavy  
 chain precursor)

IT Antibodies

Probes (nucleic acid)  
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);  
 ANST (Analytical study); BIOL (Biological study); USES (Uses)  
 (sequence and therapeutic applications for human  
 growth-assocd. protease inhibitor heavy  
 chain precursor)

IT 249916-69-6  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (amino acid sequence; sequence and therapeutic  
 applications for human growth-assocd.  
 protease inhibitor heavy chain precursor)

IT 249916-73-2  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (nucleotide sequence; sequence and therapeutic  
 applications for human growth-assocd.  
 protease inhibitor heavy chain precursor)

IT 249760-99-4, PN: WO9957140 SEQID: 3 unclaimed protein 249761-00-0, PN:  
 WO9957140 SEQID: 4 unclaimed protein 249761-01-1, PN: WO9957140 SEQID: 5  
 unclaimed protein  
 RL: PRP (Properties)  
 (unclaimed protein sequence; sequence and  
 therapeutic applications for human growth-assocd.  
 protease inhibitor heavy chain precursor)

LS ANSWER 6 OF 15 MEDLINE DUPLICATE 3  
 ACCESSION NUMBER: 2000012988 MEDLINE  
 DOCUMENT NUMBER: 20012988 PubMed ID: 10544273  
 TITLE: Multiple sites of proteolytic cleavage to release soluble  
 forms of hepatocyte growth factor activator inhibitor type  
 1 from a transmembrane form.  
 AUTHOR: Shimomura T; Denda K; Kawaguchi T; Matsumoto K; Miyazawa K;  
 Kitamura N  
 CORPORATE SOURCE: Research Center, Mitsubishi Chemical Corp., Kamoshida,  
 Aoba-ku, Yokohama, 227-8502, Japan.  
 SOURCE: JOURNAL OF BIOCHEMISTRY, (1999 Nov) 126 (5) 821-8.  
 Journal code: 0376600. ISSN: 0021-924X.  
 PUB. COUNTRY: Japan  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200002  
 ENTRY DATE: Entered STN: 20000229  
 Last Updated on STN: 20000229  
 Entered Medline: 20000214

AB Hepatocyte growth factor activator inhibitor type 1 (HAI-1) is a  
 Kunitz-type serine protease inhibitor, which was  
 identified as a potent inhibitor of hepatocyte growth factor  
 (HGF) activator from the conditioned medium of a human carcinoma  
 cell line. HGF activator is a blood coagulation factor XII-like serine  
 protease that is responsible for proteolytic activation of the inactive  
 single chain precursor of HGF in injured tissues. The predicted  
 sequence of the primary translation product of HAI-1, which has a  
 hydrophobic sequence in its COOH-terminal region, suggested that  
 HAI-1 is first produced in a membrane-associated form. In this study, we  
 identified a transmembrane form of HAI-1 integrated in the plasma membrane  
 of cultured cells using a monoclonal antibody against HAI-1. We also  
 identified several soluble forms of HAI-1 in the conditioned medium of the  
 cells, indicating that multiple sites are present in the transmembrane  
 form of HAI-1 at which proteolytic cleavage releases the extracellular  
 domain. At least two proteases, one of which is a metalloprotease, appear  
 to be responsible for the release. Further, the soluble forms of HAI-1  
 have different inhibitory activity against HGF activator. These findings  
 suggest that proteolytic processing plays important roles in regulation of  
 the inhibitory activity of HAI-1.

AB Hepatocyte growth factor activator inhibitor type 1 (HAI-1) is a  
 Kunitz type serine protease inhibitor, which was  
 identified as a potent inhibitor of hepatocyte growth factor  
 (HGF) activator from the conditioned medium of a human carcinoma  
 cell line. HGF activator is a blood coagulation factor XII-like serine  
 protease that is responsible for proteolytic activation of the inactive  
 single chain precursor of HGF in injured tissues. The predicted  
 sequence of the primary translation product of HAI-1, which has a  
 hydrophobic sequence in its COOH-terminal region, suggested that  
 HAI-1 is first produced in a membrane-associated form. In this study, we  
 identified a . . .

LS ANSWER 7 OF 15 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998-682507 CAPLUS  
 DOCUMENT NUMBER: 129-299030  
 TITLE: Transgenic expression in genital tract and sexual  
 accessory glands  
 INVENTOR(S): Pothier, Francois  
 PATENT ASSIGNEE(S): Universite Laval, Can.  
 SOURCE: PCT Int. Appl., 25 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9845419	A1	19981015	WO 1998-CA309	19980402
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, LZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW, GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9869140	A1	19981030	AU 1998-69140	19980402
EP 977837	A1	20000209	EP 1998-914736	19980402
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-825955 A2 19970403  
 WO 1998-CA309 W 19980402

AB The present invention relates to a method for the prodn. and secretion  
 into animal's semen of an exogenous recombinant protein comprising the  
 steps of: (a) producing a transgenic animal characterized by an expression  
 system comprising a promoter specific for the genital tract or accessory

glands operatively linked to an exogenous DNA sequence coding for the recombinant protein through a DNA sequence coding for a signal peptide effective in secreting and maturing the recombinant protein in genital tract tissue; (b) collecting semen produced by said transgenic animal; and (c) isolating the exogenous recombinant protein from the semen. Human growth hormone cDNA was placed under control of mouse secretory protease inhibitor p12 promoter sequence in a construct that included a polyA tail and a SV40 intron for stabilization of the mRNA. Transgenic mice were generated by pronuclear injection of the construct into zygotes. After mating with transgenic males, the female vaginal plug contained 30.44 ng/mL human growth hormone.

AB The present invention relates to a method for the prodn. and secretion into animal's semen of an exogenous recombinant protein comprising the steps of: (a) producing a transgenic animal characterized by an expression system comprising a promoter specific for the genital tract or accessory glands operatively linked to an exogenous DNA sequence coding for the recombinant protein through a DNA sequence coding for a signal peptide effective in secreting and maturing the recombinant protein in genital tract tissue; (b) collecting semen produced by said transgenic animal; and (c) isolating the exogenous recombinant protein from the semen. Human growth hormone cDNA was placed under control of mouse secretory protease inhibitor p12 promoter sequence in a construct that included a polyA tail and a SV40 intron for stabilization of the mRNA. Transgenic mice were generated by pronuclear injection of the construct into zygotes. After mating with transgenic males, the female vaginal plug contained 30.44 ng/mL human growth hormone.

L5 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2002 ACS  
1997:187651 CAPLUS  
ACCESSION NUMBER: 1997:187651 CAPLUS  
DOCUMENT NUMBER: 126:302999  
TITLE: Hepatocyte growth factor activator inhibitor, a novel Kunitz-type serine protease inhibitor  
AUTHOR(S): Shimomura, Takeshi; Denda, Kimitoshi; Kitamura, Akiko; Kawaguchi, Toshiya; Kito, Masahiro; Kondo, Jun; Kagaya, Shinji; Qin, Li; Takata, Hiroyuki; Miyazawa, Keiji; Kitamura, Naomi  
CORPORATE SOURCE: Research Center, Mitsubishi Chemical Corp., Yokohama, 227, Japan  
SOURCE: J. Biol. Chem. (1997), 272(10), 6370-6376  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Hepatocyte growth factor (HGF) activator is a serine protease that is produced and secreted by the liver and circulates in the blood as an inactive zymogen. In response to tissue injury, the HGF activator zymogen is converted to the active form by limited proteolysis. The activated HGF activator converts an inactive single chain precursor of HGF to a biol. active heterodimer in injured tissue. The activated HGF may be involved in the regeneration of the injured tissue. In this study, the authors purified an inhibitor of HGF activator from the conditioned medium of a human MKN45 stomach carcinoma cell line and molecularly cloned its cDNA. The sequence of the cDNA revealed that the inhibitor has two well defined Kunitz domains, suggesting that the inhibitor is a member of the Kunitz family of serine protease inhibitors. The sequence also showed that the primary translation product of the inhibitor has a hydrophobic sequence at the C-terminal region. Inhibitory activity toward HGF activator was detected in the membrane fraction as well as in the conditioned medium of MKN45 cells. These results suggest that the inhibitor may be produced as a membrane-assoccd. form and secreted by the producing cells as a proteolytically truncated form.

IT Protein sequences  
cDNA sequences  
(cDNA sequence for human hepatocyte growth factor activator inhibitor, a novel Kunitz-type serine protease inhibitor, and characterization of its inhibitory activity and tissue distribution)

IT 188701-87-3  
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)  
(amino acid sequence; cDNA sequence for human hepatocyte growth factor activator inhibitor, a novel Kunitz-type serine protease inhibitor, and characterization of its inhibitory activity and tissue distribution)

IT 189200-91-7, Hepatocyte growth factor activator inhibitor  
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)  
(cDNA sequence for human hepatocyte growth factor activator inhibitor, a novel Kunitz-type serine protease inhibitor, and characterization of its inhibitory activity and tissue distribution)

IT 149885-78-9, Hepatocyte growth factor activator  
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(cDNA sequence for human hepatocyte growth factor activator inhibitor, a novel Kunitz-type serine protease inhibitor, and characterization of its inhibitory activity and tissue distribution)

IT 189176-23-6  
RL: PRP (Properties)  
(nucleotide sequence; cDNA sequence for human hepatocyte growth factor activator inhibitor, a novel Kunitz-type serine protease inhibitor, and characterization of its inhibitory activity and tissue distribution)

L5 ANSWER 9 OF 15 MEDLINE  
ACCESSION NUMBER: 1998049419 MEDLINE  
DOCUMENT NUMBER: 98049419 PubMed ID: 9389551  
TITLE: The growth hormone dependent serine protease inhibitor, Spi 2.1 inhibits the des (1-3) insulin-like growth factor-I generating protease.  
AUTHOR: Maake C; Yamamoto H; Murphy L J  
CORPORATE SOURCE: Department of Internal Medicine, University of Manitoba, Winnipeg, Canada.  
SOURCE: ENDOCRINOLOGY, (1997 Dec) 138 (12) 5630-6.  
Journal code: 0375040. ISSN: 0013-7227.  
PUB. COUNTRY: United States  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 199712

DUPLICATE 4

ENTRY DATE: Entered STN: 19980116  
Last Updated on STN: 20000303  
Entered Medline: 19971229

AB The conversion of insulin-like growth factor-I (IGF-I) to the biologically more active des (1-3) IGF-I variant is catalyzed by a ubiquitous protease. This proteolytic activity is inhibited by **human** alaphal-antitrypsin and soy-bean trypsin inhibitor and is up-regulated in serum and tissue extracts of hypophysectomized rats. These observations lead us to investigate whether the growth hormone regulated, serine protease inhibitor, Spi 2.1 was able to inhibit the des (1-3) IGF-I generating protease. Dihydrofolate reductase deficient Chinese hamster ovary (CHO/dhfr-ve) cells were transfected with a rat Spi 2.1 expression vector containing the dhfr and neomycin resistance gene. Stable transfectants were selected using G418 and amplified using methotrexate. Conditioned medium from Spi 2.1 transfected CHO cells potently inhibited proteolytic activity directed against a synthetic hexa-peptide with a **sequence** identical to the N-terminal of IGF-I. In contrast conditioned medium from wild-type CHO cells had little effect. Based upon these observations we suggest that our previous finding of enhanced des (1-3) IGF-I generating protease activity in growth hormone deficient rats may be, at least partly explained by reduced levels of Spi 2.1. Furthermore, we propose that the regulation of the generation of des (1-3) IGF-I may be an additional potential site of growth hormone regulation of IGF-I action.

AB . . . . the biologically more active des (1-3) IGF-I variant is catalyzed by a ubiquitous protease. This proteolytic activity is inhibited by **human** alaphal-antitrypsin and soy-bean trypsin inhibitor and is up-regulated in serum and tissue extracts of hypophysectomized rats. These observations lead us to investigate whether the growth hormone regulated, serine protease inhibitor, Spi 2.1 was able to inhibit the des (1-3) IGF-I generating protease. Dihydrofolate reductase deficient Chinese hamster ovary (CHO/dhfr-ve) cells were transfected with a rat Spi 2.1 expression vector containing the dhfr and neomycin resistance gene. Stable transfectants were selected using G418 and amplified using methotrexate. Conditioned medium from Spi 2.1 transfected CHO cells potently inhibited proteolytic activity directed against a synthetic hexa-peptide with a **sequence** identical to the N-terminal of IGF-I. In contrast conditioned medium from wild-type CHO cells had little effect. Based upon these. . . .

L5 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5  
ACCESSION NUMBER: 1997793657 CAPLUS  
DOCUMENT NUMBER: 128:112241  
TITLE: The anionic protease inhibitor BWI-1 from buckwheat seeds. Kinetic properties and possible biological role  
AUTHOR(S): Dunaevsky, Yakov E.; Gladysheva, Inna P.; Pavlikova, Ekaterina B.; Belikova, Galina A.; Gladyshev, Dmitry P.; Papisova, Alia I.; Larionova, Natalja I.; Belozerky, Mikhail A.  
CORPORATE SOURCE: A. N. Belozerky Inst. of Physico-Chemical Biology, Moscow State Univ., Moscow, 119899, Russia  
SOURCE: Physiologia Plantarum (1997), 101(3), 483-488  
PUBLISHER: Munksgaard International Publishers Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Kinetic characteristics and effects on the growth of filamentous fungi of one of the main anionic protease inhibitors, BWI-1, isolated from buckwheat seeds, have been studied. The inhibition consts. of bovine trypsin, chymotrypsin and cathepsin G from **human** granulocytes with BWI-1 were found to be 1.1, 67 and 200 nM, resp. Anal. of the amino acid sequence of BWI-1 in the vicinity of the reactive site revealed its homol. to the potato proteinase inhibitor I family. It is suggested that the inability of BWI-1 to bind elastase of human granulocytes is due to the basic nature of the amino acid residue (Arg) at the P1 position in its reactive site. It was demonstrated that BWI-1 was able to suppress the germination of the spores and the growth of the mycelium of two filamentous fungi.

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L5 ANSWER 11 OF 15 MEDLINE DUPLICATE 6  
ACCESSION NUMBER: 93232057 MEDLINE  
DOCUMENT NUMBER: 93232057 PubMed ID: 847338  
TITLE: Senescent WI-38 cells fail to express EPC-1, a gene induced in young cells upon entry into the G0 state.  
AUTHOR: Pignolo R J; Cristofalo V J; Rotenberg M O  
CORPORATE SOURCE: Center for Gerontological Research, Medical College of Pennsylvania, Philadelphia 19129.  
CONTRACT NUMBER: AG00378 (NIA)  
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Apr 25) 268 (12)  
8949-57.  
PUB. COUNTRY: United States  
FILE SEGMENT: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
OTHER SOURCE: Priority Journals  
GENBANK-M90439  
ENTRY MONTH: 199305  
ENTRY DATE: Entered STN: 19930604  
Last Updated on STN: 19930604  
Entered Medline: 19930514

AB Recently we reported the isolation of cDNAs for a number of genes that are differentially expressed between nonproliferating early (young) and late (senescent) population doubling level (PDL) WI-38 human, fetal lung-derived, fibroblast-like cells. We now demonstrate that one of these isolates, EPC-1 (early PDL cDNA-1), derives from an approximately 1.4-kilobase mRNA species that is expressed at a > or 100-fold higher level in serum-starved, confluent, young versus similarly treated senescent WI-38 cells. Complete nucleotide sequence analysis of this cDNA confirms its identity with that of a cDNA encoding a secreted, retinal pigmented epithelium differentiation factor as well as similarity of the encoded protein with a number of mammalian serine protease inhibitors. We show that EPC-1 expression is associated with G0 growth arrest in WI-38 cells. The mRNA readily accumulates in

density-arrested and/or serum-starved young cells but not in log phase, low density young cells. In contrast, EPC-1 transcript abundance and expression of the encoded, secreted protein are both negligible in senescent WI-38 cells under all culture conditions tested. These findings support the hypothesis that senescent WI-38 cells exhibit a state of growth arrest fundamentally distinct from that of quiescent (G0) young cells.

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DUPLICATE 7

L5 ANSWER 12 OF 15 MEDLINE  
ACCESSION NUMBER: 92407628 MEDLINE  
DOCUMENT NUMBER: 92407628 PubMed ID: 1326608  
TITLE: Structure and chromosomal localization of the mammalian agrin gene.  
AUTHOR: Rupp F; Ozcelik T; Linial M; Peterson K; Francke U;  
Scheller R  
CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Molecular and Cellular Physiology, Stanford University School of Medicine, California 94305.  
SOURCE: JOURNAL OF NEUROSCIENCE, (1992 Sep) 12 (9) 3535-44.  
Journal code: 8102140. ISSN: 0270-6474.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-M92654; GENBANK-M92655; GENBANK-M92656;  
GENBANK-M92657; GENBANK-M92658; GENBANK-M92659  
ENTRY MONTH: 199210  
ENTRY DATE: Entered STN: 19921106  
Last Updated on STN: 19921106  
Entered Medline: 19921019

AB Agrin, a component of the synaptic basal lamina, has been shown to induce clustering of ACh receptors on the surface of muscle fibers. Analysis of cDNAs isolated from a rat embryonic spinal cord library demonstrated that agrin contains domains similar to regions of protease inhibitors, laminin and epidermal growth factor. The domain structure of agrin is further revealed here in an analysis of the agrin gene. Two additional internal repeated sequences are defined: one rich in cysteine residues with no homology to other proteins, and another similar to the laminin G domain, which is involved in heparin binding. Alternative RNA splicing at two positions in the gene predicts up to eight possible forms of the agrin protein. The gene (symbol AGRN/Agrn) has been assigned to chromosome 1 region pter-p32 in human and to mouse chromosome 4.

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DUPLICATE 8

L5 ANSWER 13 OF 15 MEDLINE  
ACCESSION NUMBER: 90015171 MEDLINE  
DOCUMENT NUMBER: 90015171 PubMed ID: 2507928  
TITLE: Protease nexin-II, a potent antichymotrypsin, shows identity to amyloid beta-protein precursor.  
AUTHOR: van Nostrand W E; Wagner S L; Suzuki M; Choi B H; Farrow J S; Geddes J W; Cotman C W; Cunningham B D  
COPORATE SOURCE: Department of Microbiology and Molecular Genetics, University of California, Irvine 92717.  
SOURCE: NATURE, (1989 Oct 12) 341 (6242) 546-9.  
Journal code: 0410462. ISSN: 0028-0836.  
PUB. COUNTRY: ENGLAND: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198911  
ENTRY DATE: Entered STN: 19900328  
Last Updated on STN: 19980206  
Entered Medline: 19891117

AB Protease nexin-II (PN-II) is a protease inhibitor that forms SDS-resistant inhibitory complexes with the epidermal growth factor (EGF)-binding protein, the gamma-subunit of nerve growth factor, and trypsin. The properties of PN-II indicate that it has a role in the regulation of certain proteases in the extracellular environment. Here we describe more of the amino-acid sequence of PN-II and its identity to the deduced sequence of the amyloid beta-protein precursor (APP). Amyloid beta-protein is present in neuritic plaques and cerebrovascular deposits in individuals with Alzheimer's disease and Down's syndrome. A monoclonal antibody against PN-II (designated mAbP2-1) recognized PN-II in immunoblots of serum-free culture medium from human glioblastoma cells and neuroblastoma cells, as well as in homogenates of normal and Alzheimer's disease brains. In addition, mAbP2-1 stained neuritic plaques in Alzheimer's disease brain. PN-II was a potent inhibitor of chymotrypsin with an inhibition constant Ki of  $6 \times 10^{-10}$ M. Together, these data demonstrate that PN-II and APP are probably the same protein. The regulation of extracellular proteolysis by PN-II and the deposition of at least parts of the molecule in senile plaques is consistent with previous reports that implicate altered proteolysis in the pathogenesis of Alzheimer's disease.

AB Protease nexin-II (PN-II) is a protease inhibitor that forms SDS-resistant inhibitory complexes with the epidermal growth factor (EGF)-binding protein, the gamma-subunit of nerve growth factor, and trypsin. The properties of PN-II indicate that it has a role in the regulation of certain proteases in the extracellular environment. Here we describe more of the amino-acid sequence of PN-II and its

identity to the deduced sequence of the amyloid beta-protein precursor (APP). Amyloid beta-protein is present in neuritic plaques and cerebrovascular deposits in individuals with Alzheimer's disease and Down's syndrome. A monoclonal antibody against PN-II (designated mAbP2-1) recognized PN-II in immunoblots of serum-free culture medium from human glioblastoma cells and neuroblastoma cells, as well as in homogenates of normal and Alzheimer's disease brains. In addition, mAbP2-1 stained.

L5 ANSWER 14 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1987:315792 BIOSIS

DOCUMENT NUMBER: BA84:35299

TITLE: STUDY OF A GROWTH HORMONE-REGULATED PROTEIN SECRETED BY RAT HEPATOCYTES COMPLEMENTARY DNA CLONING ANTI-PROTEASE ACTIVITY AND REGULATION OF ITS SYNTHESIS BY VARIOUS HORMONES.

AUTHOR(S): LE CAM A; PAGES G; AUBERGER P; LE CAM G; LEOPOLD P;

BENAROUS R; GLAICHENHAUS N

CORPORATE SOURCE: UNITE INSERM 145, FAC. MED. 06034 NICE, FR.

SOURCE: EMBO (EUR MOL BIOL ORGAN) J, (1987) 6 (5), 1225-1232.

CODEN: EMJODG. ISSN: 0261-4189.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB GHR-P63 ('growth hormone-regulated protein 63,000 daltons') is an acidic glycoprotein secreted by rat hepatocytes whose synthesis is abolished upon hypophsectomy. The sequence of its mRNA including the entire coding and 3' untranslated regions was determined from a nearly full-length lambda.gtl1-cDNA clone. The sequence contained two ATGs in frame giving rise to two overlapping coding regions which could encode precursor polypeptides of 416 and 406 amino acid residues (Mr = 46549 and 45371). These potential translation initiation codons appeared to be functional both in vitro and in intact cells since two precursors of the correct size were immunoprecipitated as products of mRNA translation. The unglycosylated precursors were converted into intermediate intracellular forms of about 56,000 daltons containing N-linked oligosaccharide side chains and thereafter into the secretory form of .simeq. 63,000 daltons. Strong sequence homologies, both at the nucleotide and the amino acid levels were found between GHR-P63 and several serum protease inhibitors, more particularly mouse contrapsin and human .alpha.1-antichymotrypsin. In agreement with sequence data, GHR-P63 purified from rat blood by affinity chromatography was found to carry an anti-trypsin activity. GHR-P63 mRNA, virtually undetectable in hepatocytes from hypophsectomized rats, could be hormonally re-induced to subnormal levels both in vivo by treating animals with hormones and in vitro by incubating the defective cells with hormones. Growth hormone was absolutely required but had a weak effect when used alone. Glucocorticoids which had no effect when used per se, strongly potentiated the action of growth hormone. Nuclear run-off experiments suggest that hormones regulated GHR-P63 mRNA levels by acting mostly, if not exclusively, on gene transcription.

IT Miscellaneous Descriptors

HUMAN ALPHA-1 ANTICHYMOTRYPSIN MOUSE CONTRAPSSIN MESSENGER RNA  
COMPLEMENTARY DNA NUCLEOTIDE SEQUENCE SERUM PROTEASE  
INHIBITORS HYPOPHSECTOMY GROWTH HORMONE

DUPLICATE 9

L5 ANSWER 15 OF 15 MEDLINE

ACCESSION NUMBER: 87156686 MEDLINE

DOCUMENT NUMBER: 87156686 PubMed ID: 2435284

TITLE: Amino-terminal sequence of a large form of basic fibroblast growth factor isolated from human benign prostatic hyperplastic tissue.

AUTHOR: Story M T; Esch F; Shimasaki S; Sasae J; Jacobs S C; Lawson R K

CONTRACT NUMBER: AM21063 (NIADDK)

SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1987

Feb 13) 142 (3) 702-9.

Journal code: 0372516. ISSN: 0006-291X.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198704

ENTRY DATE: Entered STN: 19900303

Last Updated on STN: 19970203

Entered Medline: 19870401

AB Homogenization of human benign prostatic hyperplastic tissue in high ionic strength alkaline buffer containing protease inhibitors resulted in the isolation of a 17,400 molecular weight growth factor. When tissue was homogenized in ammonium sulfate at pH 4.5 without protease inhibitors a smaller, 16,600 dalton, growth factor was isolated. Both growth factors reacted with antisera against synthetic peptides whose sequences corresponded to the amino-terminal (1-12), internal (33-43) and carboxyl-terminal (135-145) portions of basic fibroblast growth factor (bFGF). This suggested that the smaller growth factor was not a truncated form of (1-146) bFGF and that the larger growth factor may contain additional sequences. Amino-terminal sequencing showed the larger growth factor to have the sequence:  
Ala-Ala-Gly-Ser-Ile-Thr-Leu-Pro-Ala-Ile-Pro-Glu-Asp-Gly-Gly-Ser-Gly-Ala-Phe-Pro-. These results show that the larger growth factor is an 8 amino acid extended from of (1-146) bFGF and it is likely that the smaller growth factor is a proteolytic cleavage product of the larger growth factor produced during the extraction procedure.

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(FILE 'HOME' ENTERED AT 13:52:16 ON 12 JUN 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 13:52:33 ON 12 JUN 2002

L1 70323 S (PROTEASE (1N) INHIBITOR?)  
L2 912 S L1 (10N) GROWTH  
L3 212 S L2 (P) HUMAN?  
L4 35 S L3 (P) SEQUENCE?  
L5 15 DUP REM L4 (20 DUPLICATES REMOVED)

=> end ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:y  
COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
	-3.10	-3.10

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(FILE 'HOME' ENTERED AT 13:24:01 ON 12 JUN 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 13:24:18 ON 12 JUN 2002

FILE 'MEDIINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 13:24:18 ON 12 JUN 2002

3870 S HILLMAN J?/AU OR GUEGLER K?/AU OR PATTERSON C?/AU

L1 3870 S HILLMAN J?/AU OR GUEGLER K?/AU OR PATTERSON C?/AU

L2 80 S L1 AND PROTEASE?

L3 15 S L2 AND GROWTH?

L4 7 DUP REM L3 (8 DUPLICATES REMOVED)

(FILE 'HOME' ENTERED AT 13:52:16 ON 12 JUN 2002)  
(FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 13:52:33 ON 12 JUN 2002  
FILE 'PROTEASE (1N) INHIBITOR?'  
70323 S L1 (10N) GROWTH  
L1 912 S L1 (10N) GROWTH  
L2 212 S L2 (P) HUMAN?  
L3 35 S L3 (P) SEQUENCE?  
L4 15 DUP REM L4 (20 DUPLICATES REMOVED)  
L5